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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,872	12/21/2005	Nancy Hathaway	21309YP	6359

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EXAMINER	
KAROL, JODY LYNN	
ART UNIT	PAPER NUMBER
1627	
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03/12/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,872	HATHAWAY ET AL.	
	Examiner	Art Unit	
	Jody L. Karol	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/19/2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,8,11-15,20 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 7-8, 11-15, and 20-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/5/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of applicant's Amendment/Remarks filed 11/19/2009. Claims 1 and 11-15 have been amended. Claims 2-6, 9-10, and 16-19 are cancelled. Claims 1, 7-8, 11-15, and 20-21 are pending and are currently under consideration.

Information Disclosure Statement

1. The information disclosure statement (IDS) filed on 3/5/2010 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered.

WITHDRAWN REJECTIONS

2. Applicant's cancellation of claim 10 renders the rejections of claim 10 under 35 U.S.C. 103(a) as being unpatentable over Stephenson et al. (US 2004/0034083 A1) in view of Fahn et al. ("Unified Parkinson's Rating Scale") and the rejection of claim 10 under 35 U.S.C. 103(a) as being unpatentable over Teismann et al. ("Pharmacological Inhibition of COX-2 Provides Neuroprotection in the MPTP-Mouse Model of Parkinson's Disease" – cited on IDS) in view of Factor et al. ("Parkinson's disease: an open label trial of pergolide in patients failing bromocriptine therapy," *J. of Neurol. Neurosurg. Psychiatry*, 1988; 51: pgs 529-533) and in further view of Heinonen et al. ("Safety of Selegiline (Deprenyl) in the Treatment of Parkinson's Disease," *Drug Safety*, 1998 Jul; 19 (1): pgs 11-22) moot. Thus, said rejections are herein withdrawn.

3. It is noted that "the rejection of claims 1, 7-8, 10-15, and 16-21" under 35 U.S.C. 103(a) as being unpatentable over Stephenson et al. (US 2004/0034083 A1) in view of Fahn et al. ("Unified Parkinson's Rating Scale") was a typo and should have stated the "rejection of claims 1, 7-8, 10-15, and 20-21" as claims 16-19 were previously cancelled.

4. In view of Applicant's amendments to claims 1 and 12-15, the rejection of claims 1, 7-8, 12-15, and 20 under 35 U.S.C. 103(a) as being unpatentable over Teismann et al. ("Pharmacological Inhibition of COX-2 Provides Neuroprotection in the MPTP-Mouse Model of Parkinson's Disease") in view of Factor et al. ("Parkinson's disease: an open label trial of pergolide in patients failing bromocriptine therapy," *J. of Neurol. Neurosurg. Psychiatry*, 1988; 51: pgs 529-533) is herein withdrawn.

5. In view of Applicant's amendment to claim 11, the rejection of claim 11 under 35 U.S.C. 103(a) as being unpatentable over Teismann et al. ("Pharmacological Inhibition of COX-2 Provides Neuroprotection in the MPTP-Mouse Model of Parkinson's Disease" – cited on IDS) in view of Factor et al. ("Parkinson's disease: an open label trial of pergolide in patients failing bromocriptine therapy," *J. of Neurol. Neurosurg. Psychiatry*, 1988; 51: pgs 529-533) and in further view of Fahn et al. ("Unified Parkinson's Disease Rating Scale") is herein withdrawn.

REJECTIONS

6. The following rejections and/or objections are either reiterated from the previous Office Action dated 8/192009 or newly applied. They constitute the complete set of rejections and/or objections presently being applied in the instant application. The newly applied rejections are necessitated by the amendment of claims 1 and 11-15.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 7-8, 11-15 and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stephenson et al. (US 2004/0034083 A1) in view Fahn et al. ("Unified Parkinson's Disease Rating Scale" – cited on IDS).

The instant claims are directed to methods of treating Parkinson's disease, methods for treating Hoehn & Yahr Stage I-III Parkinson's disease, relieving the symptoms of Parkinson's disease, and/or ameliorating/slowing the progress of Parkinson's disease comprising administration of a therapeutically effective amount of pergolide, the COX-2 inhibitor rofecoxib, and in claims 10 and 21, additionally administrating the secondary antiparkinson agent selegiline.

Stephenson et al. teach a method of treating or inhibiting Parkinson's disease in a subject in need thereof with one or more cyclooxygenase-2 selective (COX-2) inhibitors in combination with on or more second drugs in effective amounts to treat Parkinson's disease (see abstract; title; page 3, section [0024]). Stephenson et al. further teach COX-2 inhibitors include rofecoxib (see page 5, Table 1A, B-21; page 60, Table 2, B-21) and second drugs include the dopamine agonist pergolide and/or the enzyme inhibitor selegiline (see pages 31-32, section [0028]; page 66, section [0437]). Stephenson et al. teach the combination of rofecoxib with one or more second drugs, such as pergolide or selegiline for the treatment of Parkinson's disease (see pages 32-

34, section [0029], B-21; page 61, section [0209]). Stephenson et al. further teach the subject in need thereof is typically a human subject (see page 68, section [0432]).

Stephenson et al. do not teach an exemplification of a method treating Parkinson's disease with a combination of rofecoxib, pergolide, and selegiline. Stephenson et al. also do not teach Hoehn & Yahr stage I-III Parkinson's disease is treated, as claimed in the instant claim 11.

Fahn et al. teach different rating scales for Parkinson's disease have been used in clinical studies including Hoehn and Yahr staging and UPDRS (see pages 153156). Fahn et al. teach that the Hoehn and Yahr staging ranges from I to V, wherein a stage of I is assigned to unilateral parkinsonism, stage II is to bilateral or midline Parkinson's without postural reflex involvement, stage V is the most severe stage, and wherein the first sign of impaired postural stability is indicative of stage III (see page 154).
It would have been obvious to one of ordinary skill in the art to administer rofecoxib, pergolide, and selegiline in the treatment of Parkinson's disease because rofecoxib in combination with selegiline or dopamine agonists such as pergolide is effective for the treatment or inhibition of Parkinson's disease as taught by Stephenson et al. One of ordinary skill in the art would have been motivated to administer rofecoxib, pergolide, and selegiline in patients with Parkinson's disease because a combination of anti-Parkinson's drugs is expected to have up to an additive effect. One of ordinary skill in the art would have had a reasonable expectation of success in administering rofecoxib, pergolide, and selegiline to treat Parkinson's disease because Stephenson et al. teach that rofecoxib can be combined with one or more drugs to treat Parkinson's disease,

wherein said drugs include pergolide and selegiline. It is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose *In re Kerkhoven*, 626 F.2d 846, 205, U.S.P.Q. 1069 (C.C.P.A. 1980).

In regards to claim 11, the treatment of Parkinson's disease wherein the Parkinson's disease is Hoehn & Yahr Stage I-III Parkinson's disease is obvious because, as taught by Fahn, the current evaluation of determining the stages of Parkinson's disease is well known. One of ordinary skill in the art would readily be able to evaluate patients in the early to moderate stages of Parkinson's disease and promptly start treatment in order to avoid progression to later stages of the disease.

Thus, the invention as whole would have been *prima facie* obvious to one of ordinary skill in the art at the time it was made.

9. Claims 1, 7-8, 12-15 and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Teismann et al. ("Pharmacological Inhibition of COX-2 Provides Neuroprotection in the MPTP-Mouse Model of Parkinson's Disease" – cited on IDS) in view of Factor et al. ("Parkinson's disease: an open label trial of pergolide in patients failing bromocriptine therapy," *J. of Neurol. Neurosurg. Psychiatry*, 1988; 51: pgs 529-533) and in further view of Heinonen et al. ("Safety of Selegiline (Deprenyl) in the Treatment of Parkinson's Disease," *Drug Safety*, 1998 Jul; 19 (1): pgs 11-22).

Teismann et al. teach that neuroinflammation is believed to play a deleterious role in Parkinson's disease and in its experimental model produced by MPTP (see abstract). Teismann further teach inhibition of COX-2 by rofecoxib provides significant

neuroprotection in MPTP-treated mice, and thus may be a valuable strategy for neuroprotective therapies in Parkinson's disease (see abstract).

Teismann et al. do not teach treatment of Parkinson's disease by administering pergolide and selegiline with the rofecoxib. Teismann et al. do not teach treating Parkinson's disease in a human.

Factor et al. teach treating Parkinson's disease in patients failing bromocriptine therapy by administering pergolide (see abstract). Factor et al. further teach that the efficacy of pergolide mesylate in Parkinson's disease has been well established (see page 529).

Heinonen et al. teach selegiline is widely used in the treatment of Parkinson's disease and that selegiline is generally widely tolerated in combination with other drugs (see abstract).

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat Parkinson's disease in a human by administering pergolide as taught by Factor et al., selegiline as taught by Heinonen et al., and rofecoxib as taught by Teismann et al. One of ordinary skill in the art would have been motivated to administer the combination of pergolide, selegiline and rofecoxib to treat Parkinson's disease because pergolide, selegiline and rofecoxib are taught individually in the art to be useful for treating Parkinson's disease. It is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose *In re Kerkhoven*, 626 F.2d 846, 205, U.S.P.Q. 1069 (C.C.P.A. 1980). Thus, the concomitant employment of selegiline, pergolide, and rofecoxib which are individually known to treat

Parkinson's disease for the same purpose of treating Parkinson's treatment is reasonably expected to be effective.

While Teismann et al. does not explicitly teach administering rofecoxib to a human to treat Parkinson's disease, Teismann et al. teach an experimental model of Parkinson's disease using MPTP wherein rofecoxib is demonstrated to be effective. The next logical step would be to administer rofecoxib to humans with Parkinson's disease in order to treat said disease.

Thus, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time it was made.

10. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Teismann et al. (“Pharmacological Inhibition of COX-2 Provides Neuroprotection in the MPTP-Mouse Model of Parkinson’s Disease” – cited on IDS) in view of Factor et al. (“Parkinson’s disease: an open label trial of pergolide in patients failing bromocriptine therapy,” *J. of Neurol. Neurosurg. Psychiatry*, 1988; 51: pgs 529-533) and Heinonen et al. (“Safety of Selegiline (Deprenyl) in the Treatment of Parkinson’s Disease," *Drug Safety*, 1998 Jul; 19 (1): pgs 11-22) as applied to claims 1, 7-8, 12-15, and 20-21 above, and in further view of Fahn et al. ("Unified Parkinson's Disease Rating Scale" – cited on IDS)

Teismann et al., Factor et al., and Heinonen et al. are described *supra* as applied to claims 1, 7-8, 12-15, and 20-21.

Teismann et al., Factor et al., and Heinonen et al. do not teach Hoehn & Yahr stage I-III Parkinson's disease is treated, as claimed in the instant claim 11.

Fahn et al. teach different rating scales for Parkinson's disease have been used in clinical studies including Hoehn and Yahr staging and UPDRS (see pages 153156). Fahn et al. teach that the Hoehn and Yahr staging ranges from I to V, wherein a stage of I is assigned to unilateral parkinsonism, stage II is to bilateral or midline Parkinson's without postural reflex involvement, stage V is the most severe stage, and wherein the first sign of impaired postural stability is indicative of stage III (see page 154).

It would have been obvious to one ordinary skill in the art at the time of the invention to treat Parkinson's disease wherein the Parkinson's disease is Hoehn & Yahr Stage I-III Parkinson's disease as taught by Fahn, by administering rofecoxib, pergolide, and selegiline as obvious over Teismann et al., Factor et al. and Heinonen et al. One of ordinary skill in the art would have been motivated to treat Hoehn & Yahr Stage I-III Parkinson's disease in order to avoid or delay progression to later stages of the disease. One of ordinary skill in the art would have been readily able to evaluate the patients to determine the stage of Parkinson's disease because the current evaluation of determining the stages of Parkinson's disease is well known.

Thus, the invention as whole would have been *prima facie* obvious to one of ordinary skill in the art at the time it was made.

Response to Arguments

11. Applicant's arguments filed 11/19/2009 have been fully considered but they are not persuasive. It is noted that Applicant's arguments are addressed in so much as they still read on the maintained rejections and the new ground(s) of rejection presented *supra*.

Applicant argues that Stephenson et al. do not teach or suggest the specific tripartite combination of a COX-2 inhibitor, a dopaminergic agent, and a monoamine oxidase agent, to treat or ameliorate the symptoms of Parkinson's disease, and instead provide a laundry list of COX-2 inhibitors that may be combined with a laundry list of second drugs to treat Parkinson's disease. The Applicant states that one of skill in the art would not have had any expectation that applicant's tripartite combination of a COX-2 inhibitor, a dopaminergic agent, and a monoamine oxidase agent, would successfully treat Parkinson's disease based on Stephenson et al. In response it is respectfully submitted that Stephenson et al. teach a method o f treating Parkinson's disease comprising administering rofecoxib in combination with one or more second agents, wherein the second agents include pergolide and selegiline (see abstract; page 34, Table 2, B-21). While Stephenson et al. do not exemplify rofecoxib with pergolide and selegiline, pergolide and selegiline are both taught as agents suitable for combination with rofecoxib. Thus, Stephenson et al. clearly suggests combining rofecoxib with pergolide and/or selegiline.

The Applicant further argues that Fahn et al. do not teach or suggest a combination of a COX-2 inhibitor, a dopaminergic agent, and a monoamine oxidase

agent, to treat or ameliorate the symptoms of disease. In response it is respectfully submitted that Fahn et al. is used solely for its teaching of the different stages of Parkinson's disease as claimed in the instant claim 11.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

The Applicant's further argue that Teismann et al., Factor et al., and Heinonen et al. do not teach or suggest a tripartite combination of pergolide, selegiline, and rofecoxib to treat Parkinson's disease. In response it is respectfully submitted pergolide, selegiline, and rofecoxib are taught individually by the cited prior art to treat Parkinson's disease. It is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose *In re Kerkhoven*, 626 F.2d 846, 205, U.S.P.Q. 1069 (C.C.P.A. 1980). Further, the motivation for the combination of cited references is based on the individual teachings by the prior art references citing agents useful in the treatment of Parkinson's disease and because it is expected that the combination of agents for the same purpose would have up to an additive effect. Moreover, the combination of the pergolide, selegiline, and rofecoxib taught by the prior

art to be useful in the treatment of Parkinson's disease for the same purpose of treating Parkinson's disease is reasonably expected to be effective absent evidence to the contrary.

Thus, for these reasons, Applicant's arguments are found unpersuasive. Said rejections are maintained.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jody L. Karol whose telephone number is (571)270-3283. The examiner can normally be reached on 8:30 am - 5:00 pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Jody L. Karol/

Examiner, Art Unit 1627

/Yong S. Chong/
Primary Examiner, Art Unit 1627